

**Claims**

1. A modified extracellular domain of a cytokine receptor protein, capable of being  
5 crystallized without being complexed to a ligand molecule.
2. A modified protein according to claim 1 being a homo- or heterodimeric cytokine receptor.
- 10 3. A modified protein according to claims 1 or 2 wherein at least one molecule segment which contributes to a disordered structure is deleted.
4. A modified protein according to claim 3 truncated in at least one terminal end.
- 15 5. A modified protein according to claim 4 truncated in its C-terminal end and in its N-terminal end.
6. A modified protein according to claim 5 being human growth hormone receptor (hGHR).
- 20 7. A modified human growth hormone receptor (hGHR) according to claim 6 having 31 or 33 amino acid residues removed in its N-terminal end.
8. A modified human growth hormone receptor (hGHR) according to claim 6 or 7  
25 having 3 or 4 amino acid residues removed in its C-terminal end.
9. A modified human growth hormone receptor (hGHR) according to any of claims 6 to 8 consisting of residues 32-237, 32-234 or 34-233 of the native molecule.
- 30 10. A modified human growth hormone receptor (hGHR) according to claim 9 consisting residues 32-237 of the native molecule.

11. Crystals of a receptor protein according to any of claims 1 to 10 to any of claims 1-10 suitable for binding studies with ligand candidates.
- 5 12. Crystals according to claim 11, wherein the contact surface between two molecules is between 200 to 1800 Å<sup>2</sup> (square ångström) and more preferably between 100 to 900 Å<sup>2</sup> (square ångström).
13. Crystals according to claim 11 or 12 containing at least 50 % (v/v) of a solvent  
10 acceptable for binding studies.
14. Crystals according to claim 13 containing about 60 to 80 % (v/v) of a solvent.
15. Crystals according to any of claims 11 to 14 capable of being frozen with gaseous  
15 or liquid nitrogen with maintained capacity of diffraction to at least 3.5 Å by using synchrotron radiation source.
16. Crystals according to claim 15 capable of being frozen with gaseous or liquid  
20 nitrogen with maintained capacity of diffraction to at least 3.5 Å by using synchrotron radiation source.
17. Crystals according to any of claims 11 to 16 capable of being resistant to an addition of up to 10% (v/v) of DMSO (dimethylsulfoxide) and up to 5 % (v/v) of DMF (dimethylfluoride) for at least 24 hours.  
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18. Crystals according to any of claims 11 to 17 **characterized in that** they are formed at pH between 5.0 to 8.5.
19. Crystals according to claim 18 **characterized in that** they are formed at a pH  
30 between 7.0 and 8.0.

20. Crystals according to any of claims 11 to 17 formed in the presence of one or more salts having a concentration between 0.15 M and 1.0 M.
21. Crystals according to claim 20, wherein the salt(s) is(are) selected from a group  
5 consisting of ammonium sulfate, lithium sulfate, sodium phosphate, potassium phosphate, sodium chloride, lithium chloride, ammonium acetate, sodium acetate, magnesium chloride, sodium formate and sodium citrate.
22. A method of designing drugs with cytokine receptor activity by employing the  
10 crystals according to any of claims 11 to 21 in binding studies with selected ligand candidates.
23. A method according to claim 22 involving dimerization of the receptor.
- 15 24. A method according to claims 22 or 23, wherein the crystals are soaked or co-crystallized with a solution comprising the ligands.
25. A method according to any claims 22 to 24, wherein the receptor is a modified growth hormone receptor investigated with ligands having potential growth hormone  
20 activity.
26. A method of obtaining improved cytokine receptor crystals involving the subsequent steps of:
- (i) solving the receptor three-dimensional structure complexed to a ligand by  
25 crystallographic methods,
- (ii) identifying regions of the receptor molecule which may contribute to disorder in a crystalline state,
- (iii) producing modified receptor molecules without said regions, and
- (iv) crystallizing the modified receptor without the presence of a ligand.  
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27. A method according to claim 26 involving the extracellular part of the receptor.

28. A method according to claim 26 or 27, wherein said receptor is human growth hormone receptor.

5 29. A method according to claim 28, wherein said ligand is human growth hormone.